
Intrapulmonary delivery of bone marrow-derived mesenchymal stem cells improves survival and attenuates endotoxin-induced acute lung injury in mice.

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Public Summary:

Scientific Abstract:

Recent in vivo and in vitro work suggests that mesenchymal stem cells (MSC) have anti-inflammatory properties. In this study, we tested the effect of administering MSC directly into the airspaces of the lung 4 h after the intrapulmonary administration of Escherichia coli endotoxin (5 mg/kg). MSC increased survival compared with PBS-treated control mice at 48 h (80 vs 42%; $p < 0.01$). There was also a significant decrease in excess lung water, a measure of pulmonary edema (145 ± 50 vs 87 ± 20 microl; $p < 0.01$), and bronchoalveolar lavage protein, a measure of endothelial and alveolar epithelial permeability (3.1 ± 0.4 vs 2.2 ± 0.8 mg/ml; $p < 0.01$), in the MSC-treated mice. These protective effects were not replicated by the use of further controls including fibroblasts and apoptotic MSC. The beneficial effect of MSC was independent of the ability of the cells to engraft in the lung and was not related to clearance of the endotoxin by the MSC. MSC administration mediated a down-regulation of proinflammatory responses to endotoxin (reducing TNF- α and MIP-2 in the bronchoalveolar lavage and plasma) while increasing the anti-inflammatory cytokine IL-10. In vitro coculture studies of MSC with alveolar macrophages provided evidence that the anti-inflammatory effect was paracrine and was not cell contact dependent. In conclusion, treatment with intrapulmonary MSC markedly decreases the severity of endotoxin-induced acute lung injury and improves survival in mice.

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